cof C

DOCKET NO. 17282CPA(BOT)
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of
Sachs et al
U.S. Patent 6,776,990B2
Serial No: 09/288,326
Issued: August 17, 2004
Filed: April 8, 1999

For: METHODS AND COMPOSITIONS FOR THE TREATMENT OF PANCREATITIS

Group Art Unit: 1644

Examiner: K. Clemens

Commisioner for Patents
Alexandria, VA 22313-1450

REQUEST FOR
CERTIFICATE OF CORRECTION
UNDER RULE 322 (OFFICE MISTAKE)

Dear Sir:

Please correct the above-identified patent as shown on the accompanying Certificate of Correction Form PTO-1050.

These corrections are requested for the following reasons:

IN THE SPECIFICATION:

Column 12, line 36 (page 25, line 9); delete
"SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNTQIDLIRKKMFEALENQA" and insert in place thereof
--SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNTQIDLIRKKMKEALENQA --

Column 12, line 54 (page 25, line 19); delete
"QLFNLESSLIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS"
and insert in place thereof
--QLFNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS --

Column 12, line 62 (page 25, line 23); delete

"NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVKNKEYRLATNASQAGVEK"

and insert in place thereof

--NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVVKNKEYRLATNASQAGVEK--

Column 15, line 25 (page 27, line 5); after " ataaaaaaat atgcttctgg aaataaagat aatattgtta gaaataatga tcgtgtatat" insert --attaatgtag tagttaaaaa taaagaatat aggttagcta ctaatgcatc acaggcaggc--

IN THE CLAIMS:

Column 36, lines 7 and 8, claim 18; (page 4 of amendment filed 12/22/03); delete "binge" and insert in place thereof --hinge--

Please send the Certificate to:

Allergan, Inc.
Carlos A. Fisher (T2-7H)
Intellectual Property Dept.
2525 Dupont Drive
Irvine, CA 92612

Respectfully Submitted,

Carlos A. Fisher
Registration No. 36,510
Telephone: 714/246-4920
Telecopier: 714/246-4249

Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST-CLASS MAIL WITH SUFFICIENT POSTAGE IN AN ENVELOPE ADDRESSED TO THE: CERTIFICATE OF CORRECTION-NON FEE; COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 ON 10/13/2004 Printed Name of Person Making Deposit: Bonnie Ferguson; Signature of Person Making Deposit; Bonnie Ferguson
Date: 10/13/2004

OCT 2 5 2004

PTO/SB/44 (02-01)
Approved for use through 01/31/2004. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.
Also Fom PTO-1050

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO: 6,776,990 B2

DATED: August 17, 2004

INVENTORS: Sachs et al

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE SPECIFICATION:

Column 12, line 36; delete
"SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNTQIDLIRKKMFEALENQA"
and insert in place thereof
--SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNTQIDLIRKKMKEALENQA --

Column 12, line 54; delete
"QLFNLESSLIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS"
and insert in place thereof
--QLFNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS --

Column 12, line 62; delete
"NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVKNKEYRLATNASQAGVEK"
and insert in place thereof
--NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVVKNKEYRLATNASQAGVEK--

Column 15, line 25; after " ataaaaaaat atgcttctgg aaataaagat aatattgtta gaaataatga tcgtgtatat" insert --attaatgtag tagttaaaaa taaagaatat aggttagcta ctaatgcatc acaggcaggc--

MAILING ADDRESS OF SENDER: Carlos A. Fisher (T2-7H) 17282(BOT)
Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612

PTO/SB/44 (02-01)
Approved for use through 01/31/2004. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.
Also Form PTO-1050

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO: 6,776,990 B2

DATED: August 17, 2004

INVENTORS: Sachs et al

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE CLAIMS:

Column 36, lines 7 and 8, claim 18; delete "binge" and insert in place thereof --hinge--

MAILING ADDRESS OF SENDER: Carlos A. Fisher (T2-7H) 17282(BOT)
Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612

PTO-Form 1050

OCT 2 5 2004

PTO/SB/44 (02-01)
Approved for use through 01/31/2004. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.
Also Form PTO-1050

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO: 6,776,990 B2

DATED: August 17, 2004

INVENTORS: Sachs et al

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE SPECIFICATION:

Column 12, line 36; delete
"SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNTQIDLIRKKMFEALENQA"
and insert in place thereof
--SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNTQIDLIRKKMKEALENQA --

Column 12, line 54; delete
"QLFNLESSLIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS"
and insert in place thereof
--QLFNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS --

Column 12, line 62; delete
"NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVKNKEYRLATNASQAGVEK"
and insert in place thereof
--NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVVKNKEYRLATNASQAGVEK--

Column 15, line 25; after " ataaaaaaat atgcttctgg aaataaagat aatattgtta gaaataatga tcgtgtatat" insert --attaatgtag tagttaaaaa taaagaatat aggttagcta ctaatgcatc acaggcaggc--

MAILING ADDRESS OF SENDER: Carlos A. Fisher (T2-7H) 17282(BOT)
Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612

OCT 25 2004

PTO/SB/44 (02-01)
Approved for use through 01/31/2004. OMB 0651-0033

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO: 6,776,990 B2

DATED: August 17, 2004

INVENTORS: Sachs et al

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE CLAIMS:

Column 36, lines 7 and 8, claim 18; delete "binge" and insert in place thereof --hinge--

MAILING ADDRESS OF SENDER: Carlos A. Fisher (T2-7H) 17282(BOT)
Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612

OCT 2 5 2004

person of skill in the art. It is well known that the clostridial neurotoxins have three functional domains analogous to the three elements of the present invention. For example, the BoNT/A neurotoxin light chain is present in amino acid residues 1–448 of the BoNT/A prototoxin (i.e., before nicking of the prototoxin to form the disulfide-linked dichain holotoxin); this amino acid sequence is provided below as SEQ ID NO: 7. Active site residues are underlined:

BoNT/A Light Chain (SEQ ID NO:7)

MPFVNKQFNYKDPVNGVDIAYIKIPNAGQMQPVKAFKIHNKIWV

IPERDTFTNPEEGDLNPPPEAKQVPVSYYDSTYLSTDNEKDNYLKGVTKLFERIYSTD

LGRMLLTSIVRGIPFWGGSTIDTELKVIDTNCINVIQPDGSYRSEELNLVIIGPSADI

IQFECKSFGHEVLNLTRNGYGSTQYIRFSPDFTFGFEESLEVDTNPLLGAGKFATDPA

VTLAHELIHAGHRLYGIAINPNRVFKVNTNAYYEMSGLEVSFEELRTFGGHDAKFIDS

LQENEFRLYYYNKFKDIASTLNKAKSIVGTTASLQYMKNVFKEKYLLSEDTSGKFSVD

KLKFDKLYKMLTEIYTEDNFVKFFKVLNRKTYLNFDKAVFKINIVPKVNYTIYDGFNL

RNTNLAANFNGQNTEINNMNFTKLKNFTGLFEFYKLLCVRGIITSKTKSLDKGYNK;

The heavy chain N-terminal (H_N) translocation domain is contained in amino acid residues 449–871 of the BoNT/A amino acid sequence, shown below as SEQ ID NO: 8; a gated ion channel-forming domain probably essential for the translocation activity of this peptide is underlined (see Oblatt-Montal et al., *Protein Sci.* 4:1490–1497(1995), hereby incorporated by reference herein.

ALNDLCIKVNNWDLFFSPSEDNFTNDLNKGEEITSDTNIEAAEENISLDLIQQYYLTFNF

DNEPENISIENLSSDIIGQLELMPNIERFPNGKKYELDKYTMFHYLRAQEFEHGKSRI

ALTNSVNEALLNPSRVYTFFSSDYVKKVNKATEAAMFLGWVEQLVYDFTDETSEVSTT

DKIADITIIIPYIGPALNIGNMLYKDDFVGALIFSGAVILLEFIPEIAIPVLGTFALV

SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNYQIDLIRKKMKEALENQA

EATKAIINYQYNQYTEEEKNNINFNIDDLSSKLNESINKAMININKFLNQCSVSYLMN

SMIPYGVKRLEDFDASLKDALLKYIYDNRGTLIGQVDRLKDKVNNTLSTDIPFQLSKY

VDNQRLLSTFTEYIK;

The heavy chain C-terminal neural cell binding domain is contained in amino acid residues 872–1296 (SEQ ID NO: 9) of the BoNT/A prototoxin.

NIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQI

QLFNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS

GWKVSLNYGEIIWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNNRLNNSKIY

INGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIKYFNLFDKELNEKEIKDLY

DNQSNSGILKDFWGDYLQYDKPYYMLNLYDPNKYVDVNNVGIRGYMYLKGPRGSVMTT

NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVVKNKEYRLATNASQAGVEK

ILSALEIPDVGNLSQVVVMKSKNDQGITNKCKMNLQDNNGNDIGFIGFHQFNNIAKLV

ASNWYNRQIERSSRTLGCSWEFIPVDDGWGERPL

The amino acid sequence of the BoNT/A prototoxin is encoded by nucleotides 358 to 4245 of the neurotoxin cDNA sequence, set forth herein below as SEQ ID NO: 10.

ALNDLCIKVNNWDLFFSPSEDNFTNDLNKGEEITSDTNIEAAEENISLDLIQQYYLTFNF
DNEPENISIENLSSDIIGQLELMPNIERFPNGKKYELDKYTMFHYLRAQEFEHGKSRI
ALTNSVNEALLNPSRVYTFFSSDYVKKVNKATEAAMFLGWVEQLVYDFTDETSEVSTT
DKIADITIIIPYIGPALNIGNMLYKDDFVGALIFSGAVILLEFIPEIAIPVLGTFALV
SYIANKVLTVQTIDNALSKRNEKWDEVYKYIVTNWLAKVNTQIDLIRKKMKEALENQA
EATKAIINYQYNQYTEEEKNNINFNIDDLSSKLNESINKAMININKFLNQCSVSYLMN
SMIPYGVKRLEDFDASLKDALLKYIYDNRGTLIGQVDRLKDKVNNTLSTDIPFQLSKY
VDNQRLLSTFTEYIK;

The heavy chain C-terminal neural cell binding domain is contained in amino acid residues 872-1296 (SEQ ID NO: 9) of the BoNT/A prototoxin.

NIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQI
QLFNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCMENNS
GWKVSLNYGEIIWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNNRLNNSKIY
INGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIKYFNLFDKELNEKEIKDLY
DNQSNSGILKDFWGDYLQYDKPYYMLNLYDPNKYVDVNNVGIRGYMYLKGPRGSVMTT
NIYLNSSLYRGTKFIIKKYASGNKDNIVRNNDRVYINVVVKNKEYRLATNASQAGVEK
ILSALEIPDVGNLSQVVVMKSKNDQGITNKCKMNLQDNNGNDIGFIGFHQFNNIAKLV
ASNWYNRQIERSSRTLGCSWEFIPVDDGWGERPL

The amino acid sequence of the BoNT/A prototoxin is encoded by nucleotides 358 to 4245 of the neurotoxin cDNA sequence, set forth herein below as SEQ ID NO: 10.

aagcttctaa atttaaatta ttaagtataa atccaaataa acaatatgtt caaaaacttg
atgaggtaat aatttctgta ttagataata tggaaaaata tatagatata tctgaagata
atagattgca actaatagat aacaaaaata acgcaaagaa gatgataatt agtaatgata
tatttatttc caattgttta accctatctt ataacggtaa atatatatgt ttatctatga
aagatgaaaa ccataattgg atgatatgta ataatgatat gtcaaagtat ttgtatttat
ggtcatttaa ataattaata atttaattaa ttttaaatat tataagaggt gttaaatatg
ccatttgtta ataaacaatt taattataaa gatcctgtaa atggtgttga tattgcttat
ataaaaattc caaatgcagg acaaatgcaa ccagtaaaag cttttaaaat tcataataaa
atatgggtta ttccagaaag agatacattt acaaatcctg aagaaggaga tttaaatcca
ccaccagaag caaaacaagt tccagtttca tattatgatt caacatattt aagtacagat
aatgaaaaag ataattattt aaagggagtt acaaaattat ttgagagaat ttattcaact
gatcttggaa gaatgttgtt aacatcaata gtaaggggaa taccattttg gggtggaagt
acaatagata cagaattaaa agttattgat actaattgta ttaatgtgat acaaccagat
ggtagttata gatcagaaga acttaatcta gtaataatag gaccctcagc tgatattata
cagtttgaat gtaaaagctt tggacatgaa gttttgaatc ttacgcgaaa tggttatggc
tctactcaat acattagatt tagcccagat tttacatttg gttttgagga gtcacttgaa

-continued

gtatcatata ttgcgaataa ggttctaacc gttcaaacaa tagataatgc tttaagtaaa

agaaatgaaa aatgggatga ggtctataaa tatatagtaa caaattggtt agcaaaggtt

aatacacaga ttgatctaat aagaaaaaaa atgaaagaag ctttagaaaa tcaagcagaa

gcaacaaagg ctataataaa ctatcagtat aatcaatata ctgaggaaga gaaaaataat

attaatttta atattgatga tttaagttcg aaacttaatg agtctataaa taaagctatg

attaatataa ataaattttt gaatcaatgc tctgtttcat atttaatgaa ttctatgatc

ccttatggtg ttaaacggtt agaagatttt gatgctagtc ttaaagatgc attattaaag

tatatatatg ataatagagg aactttaatt ggtcaagtag atagattaaa agataaagtt

aataatacac ttagtacaga tatacctttt cagctttcca aatacgtaga taatcaaaga

ttattatcta catttactga atatattaag aatattatta atacttctat attgaattta

agatatgaaa gtaatcattt aatagactta tctaggtatg catcaaaaat aaatattggt

agtaaagtaa attttgatcc aatagataaa aatcaaattc aattatttaa tttagaaagt

agtaaaattg aggtaatttt aaaaaatgct attgtatata atagtatgta tgaaaatttt

agtactagct tttggataag aattcctaag tattttaaca gtataagtct aaataatgaa

tatacaataa taaattgtat ggaaaataat tcaggatgga aagtatcact taattatggt

gaaataatct ggactttaca ggatactcag gaaataaaac aaagagtagt ttttaaatac

agtcaaatga ttaatatatc agattatata aacagatgga tttttgtaac tatcactaat

aatagattaa ataactctaa aatttatata aatggaagat taatagatca aaaaccaatt

tcaaatttag gtaatattca tgctagtaat aatataatgt ttaaattaga tggttgtaga

gatacacata gatatatttg gataaaatat tttaatcttt ttgataagga attaaatgaa

aaagaaatca aagatttata tgataatcaa tcaaattcag gtattttaaa agacttttgg

ggtgattatt tacaatatga taaaccatac tatatgttaa atttatatga tccaaataaa

tatgtcgatg taaataatgt aggtattaga ggttatatgt atcttaaagg gcctagaggt

agcgtaatga ctacaaacat ttatttaaat tcaagtttgt ataggggac aaaatttatt

ataaaaaaat atgcttctgg aaataaagat aatattgtta gaaataatga tcgtgtatat

gtagaaaaaa tactaagtgc attagaaata cctgatgtag gaaatctaag tcaagtagta

gtaatgaagt caaaaaatga tcaaggaada acaaataaat gcaaaatgaa tttacaagat

aataatggga atgatatagg ctttatagga tttcatcagt ttaataatat agctaaacta

gtagcaagta attggtataa tagacaaata gaaagatcta gtaggacttt gggttgctca

tgggaattta ttcctgtaga tgatggatgg ggagaaaggc cactgtaatt aatctcaaac

tacatgagtc tgtcaagaat tttctgtaaa catccataaa aattttaaaa ttaatatgtt

taagaataac tagatatgag tattgtttga actgcccctg tcaagtagac aggtaaaaaa

ataaaaatta agatactatg gtctgatttc gatattctat cggagtcaga ccttttaact

tttcttgtat ccttttgta ttgtaaaact ctatgtattc atcaattgca agttccaatt

agtcaaaatt atgaaacttt ctaagataat acatttctga ttttataatt tcccaaaatc

cttccatagg accattatca atacatctac caactcgaga catactttga gttgcgccta

tctcattaag tttattcttg aaagatttac ttgtatattg aaaaccgcta tcactgtgaa

aaagtggact agcatcagga ttggaggtaa ctgctttatc aaaggtttca aagacaagga

cgttgttatt tgattttcca agtacatagg aaataatgct attatcatgc aaatcaagta

tttcactcaa gtacgccttt gtttcgtctg ttaac

insert
× missing line

missing on issued patent

attaatgtag tagttaaaaa taaagaatat aggttagcta ctaatgcatc acaggcaggc
gtagaaaaaa tactaagtgc attagaaata cctgatgtag gaaatctaag tcaagtagta
gtaatgaagt caaaaaatga tcaaggaata acaaataaat gcaaaatgaa tttacaagat
aataatggga atgatatagg ctttatagga tttcatcagt ttaataatat agctaaacta
gtagcaagta attggtataa tagacaaata gaaagatcta gtaggacttt gggttgctca
tgggaattta ttcctgtaga tgatggatgg ggagaaaggc cactgtaatt aatctcaaac
tacatgagtc tgtcaagaat tttctgtaaa catccataaa aattttaaaa ttaatatgtt
taagaataac tagatatgag tattgtttga actgcccctg tcaagtagac aggtaaaaaa
ataaaaatta agatactatg gtctgatttc gatattctat cggagtcaga ccttttaact
tttcttgtat ccttttttgta ttgtaaaact ctatgtattc atcaattgca agttccaatt
agtcaaaatt atgaaacttt ctaagataat acatttctga ttttataatt tcccaaaatc
cttccatagg accattatca atacatctac caactcgaga catactttga gttgcgccta
tctcattaag tttattcttg aaagatttac ttgtatattg aaaaccgcta tcactgtgaa
aaagtggact agcatcagga ttggaggtaa ctgctttatc aaaggtttca aagacaagga
cgttgttatt tgattttcca agtacatagg aaataatgct attatcatgc aaatcaagta
tttcactcaa gtacgccttt gtttcgtctg ttaac

Of course, three distinct domains analogous to those described above for BoNT/A exist for all the BoNT subtypes as well as for TeNT neurotoxin; an alignment of the amino acid sequences of these holotoxins will reveal the sequence coordinates for these other neurotoxin species.

Preferably, the translocation element and the binding element of the compositions of the present invention are separated by a spacer moiety that facilitates the binding element's binding to the desired cell surface receptor. Such a spacer may comprise, for example, a portion of the BoNT Hc sequence (so long as the portion does not retain the ability to bind to motor neurons or sensory afferent neurons), another sequence of amino acids, or a hydrocarbon moiety. The spacer moiety may also comprise a proline, serine, threonine and/or cysteine-rich amino acid sequence similar or identical to a human immunoglobulin hinge region. In a preferred embodiment, the spacer region comprises the amino acid sequence of an immunoglobulin γ1 hinge region; such a sequence has the sequence (from N terminus to C terminus):

8. The composition of claim 5 wherein said binding element comprises an amino acid sequence consisting of SEQ ID NO: 6.

9. The composition of claim 8 wherein said binding element comprises an amino acid sequence consisting of SEQ ID NO: 5.

10. The composition of claim 9 wherein said binding element comprises an amino acid sequence consisting of SEQ ID NO: 4.

11. The composition of claim 10 wherein said binding element comprises an amino acid sequence consisting of SEQ ID NO: 3.

12. The composition of claim 11 wherein said binding element comprises an amino acid sequence consisting of SEQ ID NO:2.

13. The composition of claim 1 wherein said composition further comprises a spacer moiety separating said binding element from said translocation element.

14. The composition of claim 13 wherein said spacer moiety comprises a moiety selected from the group consisting of a hydrocarbon, a polypeptide other than an immunoglobulin hinge region, and a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

15. The composition of claim 14 wherein said spacer moiety comprises a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

16. The composition of claim 15 wherein said polypeptide comprises an amino acid sequence consisting of SEQ ID NO:11.

17. The composition of claim 7 wherein said composition further comprises a spacer moiety separating said binding element from said translocation element.

18. The composition of claim 17 wherein said spacer moiety comprises a moiety selected from the group consisting of a hydrocarbon, a polypeptide other than an immunoglobulin binge region, and a proline-containing polypeptide identical or analogous to an immunoglobulin binge region.

19. The composition of claim 18 wherein said spacer moiety comprises a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

20. The composition of claim 19 wherein said polypeptide comprises an amino acid sequence consisting of SEQ ID NO:11.

21. The composition of claim 8 wherein said composition further comprises a spacer moiety separating said binding element from said translocation element.

22. The composition of claim 17 wherein said spacer moiety comprises a moiety selected from the group consisting of a hydrocarbon, a polypeptide other than an immunoglobulin hinge region, and a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

23. The composition of claim 18 wherein said spacer moiety comprises a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

24. The composition of claim 19 wherein said polypeptide comprises an amino acid sequence consisting of SEQ ID NO:11.

* * * * *

17. (Original) The composition of claim 7 wherein said composition further comprises a spacer moiety separating said binding element from said translocation element.

18. (Original) The composition of claim 17 wherein said spacer moiety comprises a moiety selected from the group consisting of a hydrocarbon, a polypeptide other than an immunoglobulin hinge region, and a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

19. (Original) The composition of claim 18 wherein said spacer moiety comprises a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

20. (Original) The composition of claim 19 wherein said polypeptide comprises an amino acid sequence consisting of SEQ ID NO:11.

21. (Original) The composition of claim 8 wherein said composition further comprises a spacer moiety separating said binding element from said translocation element.

22. (Original) The composition of claim 17 wherein said spacer moiety comprises a moiety selected from the group consisting of a hydrocarbon, a polypeptide other than an immunoglobulin hinge region, and a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

23. (Original) The composition of claim 18 wherein said spacer moiety comprises a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

24. (Original) The composition of claim 19 wherein said polypeptide comprises an amino acid sequence consisting of SEQ ID NO:11.

25-50 (Cancelled)